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综述

基于3.0 T高分辨率磁共振成像的大脑中动脉粥样硬化性狭窄研究进展

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摘要:颅内动脉粥样硬化性疾病(intracranial atherosclerotic disease, ICAD)是国人缺血性卒中主要原因,防治难点在于卒中高危人群筛查及有效治疗方法的选择(药物治疗/介入治疗)。3.0 T HR MRI具有在体、无创、无电离辐射等优势,能够从管壁结构及斑块特性的视角筛选大脑中动脉(middle cerebral artery, MCA)粥样硬化狭窄的卒中高危因素,观察疾病进程和临床疗效,具有潜在的预判介入手术获益人群的优势,临床应用前景广阔。目前HR MRI在MCA狭窄患者评估中的应用研究主要集中在方法学可行性、诊断与鉴别诊断、病因学等3方面,缺乏临床疗效评估及预后因素分析(尤其是术后再狭窄)相关实践,值得深入探讨。
关键词:颅内动脉狭窄;动脉粥样硬化;高分辨MR管壁成像;大脑中动脉;斑块;血管壁

Intracranial atherosclerotic middle cerebral arterial stenosis research based on 3.0 Tesla high-resolution magnetic resonance imaging: recent progress

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Abstract: Intracranial atherosclerotic disease (ICAD) of a major intracranial artery, including middle cerebral artery (MCA), basilar artery, is the most common causes of stroke and is associated with a high risk of recurrent stroke in China. The difficulty to treatment these high-risk disease is to identify high-risk stroke subgroups and to develop more effective treatments (aggressive medical therapy/endovascular therapy). With the benefits, including non-invasive, in vivo, and no-ionizing radiation, 3.0 Tesla high-resolution magnetic resonance imaging (HR MRI) could be used to stratify high-risk patients, monitor progression of disease, and evaluate clinical efficacy, based on MCA wall structure and plaque characteristic. HR MRI has the latency of predicting high-risk patients benefit from endovascular therapy, having a broad application prospect during psot-SAMMPRIS era. The current research on MCA stenosis using HR MRI focuses on methodology, diagnosis and differential diagnosis, etiology, and lacks of clinical efficiency evaluation and prognostic analysis of ICAD treatment, especially lacks the research on in-stent restenosis, which needs further investigation.
Key words: intracranial arterial stenosis; atherosclerosis; high-resolution magnetic resonance imaging; middle cerebral artery; plaque; vessel wall

颅内动脉粥样硬化性疾病(ICAD)是国人缺血性卒中的最主要病因,严重威胁国人健康[1-3]。动脉粥样硬化可累及所有的颅内血管,其中大脑中动脉(middle cerebral artery, MCA)因血供范围广,最易受累[1-3]。MCA狭窄或闭塞病变所致国人缺血性脑卒中事件甚至高达50%[3],且具有较高的卒中复发率及高残死率[4-8]。因此,科学预防、早期诊断、有效治疗ICAD所致缺血性卒中对国人健康至关重要。

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近年来,随着磁共振扫描技术的进步及新型线圈的应用,高分辨率磁共振成像(high-resolution magnetic resonance imaging, HR MRI)被应用于颈动脉粥样硬化性狭窄血管管壁结构分析及斑块成分的判断,能够无创显示管壁结构、检测斑块成分,取得了显著成效。其在颈动脉粥样硬化狭窄的成功经验给在体无创显示颅内粥样硬化性狭窄血管管壁及斑块带来了希望,逐渐成为颅内动脉狭窄研究的热点,被应用于颅内MCA、BA狭窄评估,被认为是目前唯一能在体进行颅内血管管壁成像研究的方法[9],具有广阔的应用前景。因此,本文首次就HR MRI评判MCA狭窄研究最新进展进行全面系统综述,供同行参考。

1 HR MRI成像技术进展

与传统的DSA、CTA、MRA等传统影像检查相比,

HR MRI评估动脉粥样硬化性MCA狭窄的优势主要包括定量、定性分析两个方面,即病变血管管壁厚度、斑块负荷等形态学的测量以及不同斑块成分、斑块稳定性的区别[10-11]。由于颅内血管部位深在、管径较小,为达到上述两个目的,在传统T_1WI/T_2WI序列的基础上,HR MRI必须通过改进设备、更新软件解决3个方面的难题:(1)提供足够的空间分辨率以清楚显示病变区域;(2)能够有效对比区分病变血管管壁及斑块不同成分;(3)能够有效排除潜在的信号干扰因素,包括心脏搏动、呼吸、血流、患者不自主移动等。

1.1 空间分辨率的提高

由于颈动脉管壁较厚、位置表浅,1.5 T HR MRI就可以获得较清晰的管壁图像,达到分析要求[12]。因此,早期颅内狭窄动脉HR MRI研究也采用1.5 T HR MRI设备,取得初步成效,但图像分辨率低,无法准确分辨MCA管壁结构及斑块成分[13]。高场强3.0 T HR MRI设备的应用,提高了信噪比(signal to noise ratio, SNR),进一步采用多通道头部线圈可以进一步提高SNR,显著提高了图像空间分辨率,提高了成像质量[14]。更高场强(7.0 T[15-16]、9.4 T[17])的HR MRI设备也已问世,在体外[17]及动物模型[15]中进行了初步应用,获得了较好的图像[18],但设备安全性有待确认,尚不能在临床常规使用。

此外,随着扫描技术及后处理软件的不断发展,目前HR MRI MCA管壁成像多采用多序列对比成像技术,主要包括T_2加权成像(T_2WI)、T_1加权成像(T_1WI)、质子密度加权成像(PDWI)、短时间反转恢复序列(STIR)、时间飞跃法(TOF)等序列,不同序列MRI图像空间分辨率不尽相同,其中T_2WI图像具有较高的图像分辨率,被推荐用于MCA管壁、斑块定量分析[19]。

1.2 组织对比度的提升

动脉粥样斑块成分复杂,包含脂核、纤维帽、钙化、血栓、出血等,区分困难[12, 20-21]。多序列对比成像技术不仅可部分提高图像空间分辨率,更是区分不同组织成分、提高组织对比度的关键。与常规MRI T_2WI、T_1WI序列不同,HR MRI独特的"亮血"[22]、"黑血"[23]技术能提高血液与管壁及斑块的对比度,有效区分狭窄血管的管腔及管壁。"亮血技术"即3D-TOF MRA,使血流信号显示为高信号,斑块为低信号,在冠脉、颈动脉狭窄斑块研究中具有重要意义,能够有效区分管壁与血流及不同斑块成分[22, 24],但对颅内狭窄MCA成像效果较差,常过高评价狭窄程度,可能与MCA部位深在、管径较小等因素有关。

"黑血"技术的应用部分解决了这一问题。"黑血"技术采用空间预饱和脉冲、流空效应降低血流信号,突出显示斑块和管壁,且不受血液湍流影响,避免了3D-TOF过高评价血管狭窄程度的缺点。"黑血"技术还有效采用双反转恢复自旋回波(double inversion recovery spin echo, DIR SE)及快速自旋回波(turbo spin echo, TSE)技术获得T_1WI、T_2WI、PDWI,有效提高相对SNR及组织对比度,是颈动脉斑块分析的常用序列[23]。不同序列各有优势,T_1WI、T_2WI能较好地区分斑块成分,利于定性分析,而PDWI能较好地区分管壁和管腔,利于定量分析。因此,结合使用多个序列的优势,进一步采用脂肪抑制、DIR超快速场回波(turbo field echo, TFE)等技术,可缩短扫描时间,提高图像质量及组织对比度,有利于有效分析颅内MCA狭窄管壁结构及斑块成分。

此外,有效对比剂的应用也有利于提高组织对比度。目前临床主要采用顺磁性对比剂增强扫描以增加不同组织之间的对比,能够对平扫不易确定的斑块成分(如纤维组织、钙化斑块、新生血管等)进行有效区分,有助于确定斑块成分及稳定性[25-26]。钆喷酸葡甲胺(gadopentetate dimeglumine, Gd)增强剂有利于对脂质坏死核心、纤维基质、纤维帽等定量定性分析,还能显示斑块内新生血管生成及炎症情况,被用于临床增强扫描以判断颅内血管斑块稳定性[25-27]。新型的超微顺磁铁氧化物(ultrasmall particles of iron oxide, USPIO)由于生物半衰期长,能够被斑块中巨噬泡沫细胞摄取,T_2WI呈现低信号,被用于研究不同斑块成分及斑块炎症反应,在颈动脉斑块研究中取得初步成效[28-29],但目前尚未被用于颅内血管成像。

1.3 抗干扰能力的增强

相比颈动脉HR MRI检查,MCA管壁成像更易受呼吸、心脏搏动、周围组织结构、患者耐受性等的影响。因此,提高MCA HR MRI检查的抗干扰能力对其临床应用具有重要意义。HR MRI检查扫描时间较长,很多患者难以忍受,即使坚持完成扫描,也无法保证呼吸、心率平稳,是干扰HR MRI图像质量的主要因素。因此,MCA管壁成像检查时应根据血管病变情况选择合适序列进行针对性扫描,在保证高SNR及较高空间分辨率的基础上,尽量缩短成像时长,如目前采用的FSE-T_2WI序列。相信随着扫描技术的进步和成像软件的发展,MCA管壁成像扫描时间会越来越短。MCA部位深在,周围组织结构复杂,尤其是脂肪组织对成像质量有较大的影响。由于粥样斑块内脂肪组织成分与外周脂肪三酰甘油成分不同[30],HR MRI影像学特点也不尽相同。因此,目前常采用脂肪抑制技术(STIR序列)以排除周围脂肪组织对成像的干扰。此外,呼吸、心率的波动对MCA管壁成像质量的影响也不容忽视,尤其对一些粥样硬化程度不重的患者。冠脉、颈动脉管壁成像的经验提示心电门控、呼吸导航技术的应用可以部分解决此问题,但会增加扫描时间[12, 21, 26]。因此,MCA管壁成像更多依赖患者自身配合,对一些老年依从性较差的患者,成像质量仍有待进一步提高。

2 HR MRI MCA管壁成像诊断效能研究

2.1 MCA狭窄程度的评估

管腔狭窄程度是目前症状性MCA狭窄临床诊治及预后评判的重要依据,也与脑血管事件发生密切相关,对临床诊治措施的选择至关重要[6, 31-34]。HR MRI评判颅内狭窄的突出优势是能在体无创显示管壁结构及斑块成分,但其对管腔狭窄程度的评估能力未能得到有效评价[13, 19]。因此,以DSA为金标准,以MRA、CTA为参照的HR MRI评估MCA狭窄程度的对比研究逐渐引起重视。初步的研究结果表明,HR MRI评估MCA中重度狭窄(50%~99%)及闭塞病变的敏感性、特异度要高于CTA MIP(maximum intensity projection)及CTA VR(volume rendering)成像(80.0% *vs* 53.6%、72.2%;72.7% *vs* 77.8%、18.2%),且与DSA测量结果的相关性也优于后两者(Spearman R=0.68 *vs* 0.45、0.22)[19],与DSA检测结果有较好的一致性。当然,DSA仍是目前颅内血管狭窄程度判断的金标准,HR MRI评估MCA狭窄程度可作为重要的补充手段,相关结论仍有待进一步研究证实。

2.2 MCA狭窄程度评估的可重复性研究

HR MRI评估结果的稳定性是评判其技术可行性的重要指标,只有稳定性好的技术才能得出可信的结果,并得到临床推广。颈动脉1.5 T HR MRI检查的可重复研究表明:高分辨率MRI定量、定性分析结果均具有较好的可重现性,但其对纤维帽的诊断分歧较大,仍有待进一步提高[35]。3.0 T HR MRI评估MCA粥样硬化狭窄的重现性研究表明,观察者自身(intra-observer)及不同观察者间(inter-observer)对斑块有无、斑块内出血、纤维帽等判断具有较好的一致性,但对血管面积(vessle area, VA)、管壁面积(wall area, WA)的测量以及对血液界面及脑脊液界面的定义等方面差异偏大,但仍在可接受范围内[36],提示HR MRI评判颅内狭窄(包括MCA、BA)具有较好的稳定性[3, 13, 19, 37-38]。但是,目前相关研究主要集中在基底动脉,关于MCA的可重复性研究内容较少,值得进一步深入。

2.3 MCA斑块成分辨别的可信度研究

颈动脉斑块的研究[39-40]证实,易损性斑块的破裂、脱落常导致缺血性事件的发生,与临床症状及预后密切相关[41]。颅内动脉狭窄,包括MCA、BA,由于解剖位置较深,管径较小,周围结构复杂,进行病理对照研究较困难,严重制约了HR MRI的临床应用。

目前关于颅内狭窄动脉粥样斑块成分HR MRI信号辨别依据均来自于颈动脉及冠脉斑块的经验,缺乏直接的关于颅内动脉斑块的直接证据。Klein等[42]较早对123例单侧MCA狭窄所致致死性脑梗死患者脑组织进行病例对照尸体解剖研究,比较病变侧与对侧斑块形成情况,探讨斑块形成与中重度狭窄所致脑卒中发生的关系,结果证实斑块形成与责任病变MCA中重度狭窄密切相关,提示HR MRI评价管壁、斑块对明确卒中病因的可靠性及重要性。然而,限于MCA解剖部位及图像空间分辨率,目前的HR MRI检查多数情况下仍无法有效分辨斑块纤维帽及脂质核心。早期Swartz等[43]采用T_2WI、T_1WI平扫及增强扫描进行颅内血管病变的检查,发现粥样硬化病变大多存在管壁增厚,主要表现为偏心斑块及不同程度增强表现,MCA大斑块表面明显增强,推测为纤维帽。Xu等[3]的研究发现部分MCA斑块表面T_2WI高信号带,推测可能为纤维帽。进一步的研究[37]发现HR MRI T_1高信号(high signal on T_1-weighted fat-suppressed images, HST1)与卒中发生密切相关,提示斑块内出血。更高场强(7.0 T)HR MRI的应用可以提高图像质量,观察更详细的斑块成分[18],但仍处于起步阶段,进展缓慢,值得进一步深入研究。

3 基于HR MRI的MCA粥样硬化性狭窄诊断与鉴别诊断

MCA狭窄的病因复杂,明确MCA狭窄的不同病因有利于厘清发病机制,制定合适针对性的临床诊治措施,达到最优的临床预后。目前常用的DSA、CTA、MRA等检查对MCA狭窄的鉴别诊断能力有限,而HR MRI能够聚焦于管壁特点及斑块成分,具有明显优势。

3.1 Moyamoya病

Moyamoya病(moyamoya disease, MMD)又称烟雾病,是仅次于动脉粥样硬化的MCA闭塞病因[44-45]。其发病机制、诊治方法及临床预后与粥样硬化性MCA狭窄大相径庭,且二者有时可并发,鉴别诊断困难[46-47]。

Kim等[48]采用3.0 T HR MRI对MMD、ICAD患者MCA管壁结构及斑块特点进行对比分析,主要观察指标包括:血管外径、斑块类型、强化特点等,发现MMD患者MCA狭窄部位具有更小的血管外径,偏心斑块少见,局部增强不明显。结果表明:与ICAD常导致狭窄血管扩张性正性重构(positive remodeling, PR)[3, 38, 49]不同,烟雾病狭窄MCA整体管径较小,与病理研究结果[50-51]类似;粥样斑块狭窄偏心性斑块多见,而烟雾病向心性斑块多见;粥样斑块由于斑块成分不同,表现为混杂信号及增强后明显强化,且常伴有管壁增厚,而烟雾病MCA管壁增厚少见,强化不明显,且多表现同一信号,与以往研究[43]类似。

3.2 炎性病变

原发性或继发性脑动脉炎均可导致MCA狭窄,引起急慢性缺血性卒中[52-54],必须早期明确诊断。Swartz等[43]的研究表明:炎性病变所致MCA狭窄病变常累及双侧,管壁环形增厚并均匀性强化,狭窄血管管壁光滑,斑块少见,不同与粥样硬化性狭窄所致的偏心斑块。且患者一般年龄较小,且血液炎性指标多有异常,易于鉴别[53-54],但必须引起临床重视。

4 基于HR MRI的MCA粥样硬化性狭窄病因学分析

具有相同狭窄程度的中重度MCA狭窄患者临床症状却有较大差异,很多中重度狭窄甚至闭塞MCA狭窄患者并无任何缺血症状,有无症状MCA狭窄患者卒中风险并不相同,症状性MCA狭窄年卒中再发风险明显高于无症状患者(12.5% *vs* 2.8%)[6, 55],提示斑块特性及管壁参与了狭窄所致缺血性卒中[3, 6, 56]。Klein等[42]病理对照研究也首次证实斑块形成与责任病变MCA中重度狭窄密切相关,提出HR MRI评价管壁、斑块对明确卒中病因具有重要临床意义。因此,基于HR MRI的MCA研究有利于进行卒中风险分层,筛查卒中高危患者[3, 9, 57],进而采取针对性的防治措施。

4.1 症状性MCA狭窄的斑块负荷

由于特殊的解剖部位和特点,颅内狭窄血管斑块负荷的研究一直无法进行有效定量分析。Klein等[13, 58]最早尝试采用1.5 T HR MRI进行MCA、BA斑块及管壁定量分析,证实粥样硬化MCA、BA存在不稳定斑块及管壁异常,但图像质量仍有待提高,无法进行精确量化。随着成像设备的改进及扫描技术的进步,Ryu等[9]采用3.0 T HR MRI定量分析症状性及无症状MCA狭窄患者斑块负荷及管壁特征,证实症状性MCA狭窄患者具有更大的斑块负荷,更厚的管壁面积。后续的MCA[3, 57, 59]、BA[38]系列研究进一步证实较大的斑块负荷稳定性差,是卒中高危因素,需要进行积极干预。

4.2 症状性MCA狭窄的管壁重构模式

血管重构是狭窄血管自身的代偿选择,最早在冠脉狭窄中被发现,又称"Glagov"现象[49],包含PR、负性重构(negative remo- deling, NR)两种方式。3.0 T HR MRI的应用为颅内粥样硬化狭窄血管重构模式研究提供了契机。基于高分辨率MRI的初步研究证实颅内粥样硬化狭窄MCA[3, 9, 13, 43, 57, 59]、BA[38, 58, 60]也存在"Glagov"现象。Xu等[3]采用3.0 T HR MRI对粥样硬化性狭窄MCA进行检查,发现症状性MCA狭窄患者以PR为主,无症状性MCA狭窄患者以非正性重构为主(non-PR),与文献[57, 59]报道类似;还发现部分MRA判断中重度狭窄的MCA管壁正常或仅轻度增厚,提示NR的存在,推测可能与富含纤维成分、脂质核心较小的斑块有关[3],值得进一步研究证实。Shi等[57]的研究也证实存在PR的症状性MCA狭窄存在更多的微栓子信号(microembolic signals, MESs),可能更容易发生栓子脱落。上述颅内狭窄动脉的研究提示狭窄血管的管壁重塑模式可能会对斑块特性产生影响,与斑块稳定性相关。我们在临床实践中也发现管壁重塑模式对斑块定量分析有一定干扰,尤其对负性重塑患者,可能会低估其斑块负荷程度,应引起重视。此外,目前关于颅内狭窄血管重构模式影响因素的分析较少,是未来值得关注的研究方向,具有重要意义。

4.3 症状性MCA狭窄的斑块分布部位

与冠脉及颈动脉相比,颅内大血管(MCA、BA)走行复杂,分支较多,供应不同部位的脑组织血供[61]。颅内大血管斑块形成时常累及邻近穿支,导致缺血事件,且与支架术后穿支事件密切相关[61-63]。因此,MCA狭窄的斑块分布位置具有更重要的临床价值,但目前研究较少。仅有Xu等[62]采用3.0 T HR MRI对MCA狭窄斑块分布部位进行了分析,发现粥样斑块主要分布于前壁(44.8%)、下壁(31.7%),明显多于上壁(14.3%)、后壁(9.0%),差异有统计学意义(P<0.001);症状性MCA狭窄患者中,相比于无穿支梗死,穿支梗死血管粥样斑块更多分布于上壁(P=0.001),较少分布于前壁(P=0.038)、下壁(P=0.024)。Xu等的研究取得一定的进展,部分解释了斑块分布位置与卒中风险及穿支事件的相关性,但其分析过程中将斑块部位分为前壁、下壁、上壁、后壁,未能将临床较多见且具有重要意义的"环形斑块"纳入分析,具有一定的局限。

5 基于HR MRI的MCA粥样硬化性狭窄临床疗效及预后评判

5.1 基于HR MRI的药物治疗效果及疾病预后评价

Saam等[64]采用HR MRI观察他汀类药物对颈动脉斑块进展的影响,为期18个月的观察结果表明他汀类药物可以明显降低管壁面积,减轻斑块负荷,抑制疾病进展。颅内狭窄药物治疗效果及预后的HR MRI目前鲜见。我们在临床实践中也发现部分颅内狭窄患者经过强化抗血小板、降脂治疗后,HR MRI检查发现斑块明显变小、变稳定,提示HR MRI在颅内狭窄药物随访中具有潜在价值。

5.2 基于HR MRI的微创介入治疗效果及预后评价

由于担心支架伪影及经验缺乏,目前颅内狭窄介入治疗术后HR MRI检查及随访并未得到认可,临床应用很少。Shi等[65-66]对5例MCA狭窄血管介入治疗(2例PTA,3例Wingspan支架植入)患者进行围手术期HR MRI检查,结果发现PTA改变了MCA管壁结构,导致斑块不稳定,而Wingspan支架植入能有效恢复MCA管径,效果优于PTA,结果提示3.0T HR MRI能够清晰显示介入前后管壁及斑块变化。该研究初步证实了HR MRI用于颅内血管介入治疗疗效评估的可行性,但病例数较少,仍有待进一步研究。他们的研究认为Wingspan支架为镍钛合金,3.0 T HR MRI的自旋回波技术采用射频再聚焦可以避免图像失真和热效应[65-66]。但目前临床缺乏支架术后HR MRI的影像检查的经验,尤其缺乏支架术后即刻的HR MRI图像参照,相关研究有待进一步深入。

6 总结及展望

本文首次系统全面地综述了3.0 T HR MRI在

MCA狭窄中的应用进展。一系列的研究表明:HR MRI在ICAD研究中的应用越来越广泛,具有在体、无创、无电离辐射等优势,能够定性、定量分析MCA的斑块特点及管壁结构,有利于筛选ICAS卒中高危人群,评估药物/介入治疗效果及预后,且具有潜在预判介入手术获益人群的优势,具有广阔的应用前景。但HR MRI扫描时间长,患者很难耐受,依从性差,且图像质量易受呼吸、心脏搏动等干扰。相信随着新型材料和技术的应用,HR MRI这些缺陷能得到解决,从而更好地指导临床实践,使更多患者获益。

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